XVII.—*Arylazoglyoxalinecarboxylic Acids.*

By Robert George Fargher.

Arylazoglyoxalinecarboxylic acids have been prepared by Burian (*Ber.*, 1904, **37**, 696) by the interaction of sodium diazobenzene-*p*-sulphonate and glyoxaline-4:5-dicarboxylic acid or its 2-methyl or 2-phenyl homologues. Although the reaction involved the loss of carbon dioxide, he assumed the products to be *N*-arylazo-derivatives. Since then (T., 1919, **115**, 217, 1415; 1920, **117**, 668), it has been shown that the arylazoglyoxalines are *C*-azo- and not *N*-azo-derivatives, and that the product of the reaction between sodium glyoxalinedicarboxylate and sodium diazobenzene-*p*-sulphonate is 2-*p*-sulphobenzeneazoglyoxaline-4:5-dicarboxylic acid, and not 1-*p*-sulphobenzeneazoglyoxaline-4-carboxylic acid, as stated by Burian. Nevertheless, combination is accompanied to some extent by loss of carbon dioxide, as quantitative experiments with both glyoxalinedicarboxylic acid and its 2-methyl derivative showed, and, in view of the importance of the 4-arylazoglyoxaline-5-carboxylic acids as intermediate compounds in the synthesis of the purine ring from the glyoxaline nucleus, the reaction has now been submitted to further examination.

p-Bromobenzenediazonium chloride combines readily with 2-phenylglyoxaline-4:5-dicarboxylic acid in sodium carbonate solu-

tion, one of the carboxylic acid groups being displaced by the arylazo-group. The same product, namely, 4-p-*bromobenzeneazo-2-phenylglyoxaline-5-carboxylic acid*, is obtained when the monocarboxylic acid is substituted for the dicarboxylic acid in the reaction.

Similar results are obtained with 2-methylglyoxaline-4:5-dicarboxylic acid, although in this case the reaction appears to proceed rather more slowly.

It had been anticipated that, as the possibilities of benzidine formation had been very largely excluded, the reduction of these compounds with cold stannous chloride solution would lead to the corresponding amino-acids, and that, although subsequent transformation into the glyoxalone might be anticipated in the case of the 2-methyl derivative, unless, indeed, the presence of the adjacent carboxylic grouping proved inhibitive, in that of the 2-phenyl derivative stability might reasonably be anticipated, as it had already been ascertained that the reduction of 4-*p*-bromobenzeneazo-2-phenylglyoxaline led to a substance which almost certainly possessed the constitution 5-amino-4-(2′-amino-5′-bromophenyl)-2-phenylglyoxaline.

This has, however, proved not to be the case. The reaction follows a somewhat novel and unexpected course, the second carboxylic grouping being eliminated during the process of benzidine formation, the acids yielding the same products as the corresponding non-carboxylated glyoxalines.

In view of these results, it appeared to be of interest to examine the reduction of 2-p-*bromobenzeneazoglyoxaline-4:5-dicarboxylic acid* under similar conditions. The tendency towards benzidine formation is here sufficiently less pronounced to permit of the isolation as main product of 2-p-*bromobenzenehydrazoglyoxaline-4:5-dicarboxylic acid.*

It has already been shown that glyoxalinedicarboxylic acid and its 2-methyl homologue are not acted on by a warm mixture of nitric and sulphuric acids (T., 1919, **115**, 217). 2-Phenylglyoxaline-4:5-dicarboxylic acid reacts under these conditions, but as the composition of the product indicated that substitution had taken place only in the benzene nucleus, its further examination has been omitted.

Experimental.

4-p-*Bromobenzeneazo-2-phenylglyoxaline-5-carboxylic Acid.*

A solution of 6·8 grams of *p*-bromoaniline in 130 c.c. of 10 per cent. hydrochloric acid was diazotised with 2·88 grams of sodium

nitrite and added to an ice-cold solution of 9·23 grams of 2-phenylglyoxaline-4:5-dicarboxylic acid in 400 c.c. of water containing 67·2 grams of sodium carbonate crystals, when gradual separation of a deep orange precipitate took place. After five hours, this was collected. It consisted of the *sodium* salt of 4-p-*bromobenzeneazo-2-phenylglyoxaline-5-carboxylic acid* admixed with that of the unchanged acid. Separation was readily effected by crystallisation from water containing a little sodium carbonate, the former dissolving very sparingly in cold water. The corresponding acid was readily obtained on acidification, and was further purified by crystallisation from alcohol.

4-p-*Bromobenzeneazo-2-phenylglyoxaline-5-carboxylic acid* is insoluble in water and only very sparingly so in alcohol, from which it separates in glistening, red needles, which darken on heating above 160° and effervesce and decompose at 210° (corr.). It dissolves in sulphuric acid, with the production of an eosin-red coloration (Found: C=51·6; H=3·3; N=14·8. $C_{16}H_{11}O_2N_4Br$ requires C=51·6; H=3·0; N=15·1 per cent.).

The *sodium* salt separates from water as a felted mass of orange needles containing $3H_2O$ (Found: loss at 60° in a vacuum=12·0. $C_{16}H_{10}O_2N_4BrNa,3H_2O$ requires H_2O=11·8 per cent. In dried material, Na=5·6. $C_{16}H_{10}O_2N_4BrNa$ requires Na=5·8 per cent.). The same product was obtained when 2-phenylglyoxaline-4-carboxylic acid was substituted for the dicarboxylic acid.

Reduction.—Four grams of the acid were triturated with 25 c.c. of concentrated hydrochloric acid, and gradually treated with 14 c.c. of stannous chloride solution,* the trituration being continued until the completion of the experiment. Evolution of carbon dioxide quickly became evident. The insoluble stannichloride was collected, freed from tin by means of hydrogen sulphide, and the resulting solution evaporated to low bulk under diminished pressure, when separation of a crystalline hydrochloride took place. This was purified by recrystallisation from water containing a little hydrochloric acid, and formed colourless needles melting at 255° (corr.). This was fully identified by analysis (Found: C=45·1; H=4·0; N=13·6. Calc.: C=44·8; H=3·8; N=13·8 per cent.), by the preparation of the triacetyl derivative (Found: N=12·2. Calc.: N=12·3 per cent.), and by its reactions (T., 1919, **115**, 257) as 5-amino-4-(2′-amino-5′-bromophenyl)-2-phenylglyoxaline (T., 1920, **117**, 671).

In an attempt to characterise and compare the two products more completely, it was found that sodium acetate yielded a grey precipitate, which redissolved on adding a little acetic acid and warming,

* Prepared as described in the earlier communications.

and separated in clusters of minute needles melting at 161° (corr.). This proved to be the *monoacetate* of the base (Found: C=52·1; H=4·8; N=14·1. $C_{15}H_{13}N_4Br,C_2H_4O_2$ requires C=52·4; H=4·4; N=14·4 per cent.). Ammonium oxalate yielded a grey precipitate, which darkened rapidly on warming the solution. Addition of excess of sulphuric acid to the concentrated solution of the hydrochloride caused, on stirring, the separation of a sparingly soluble *sulphate*, which crystallised in minute, flattened prisms. Ammoniacal silver nitrate was reduced in the cold.

After separation of the above hydrochloride, no further crystalline material was obtained, as the solution decomposed rapidly on exposure.

The residue, after removal of tin from the soluble stannichlorides, amounted to only 0·5 gram, and consisted mainly of ammonium chloride, although a little *p*-bromoaniline (0·07 gram) was isolated and identified by means of the acetyl derivative.

Reduction with sodium hyposulphite in alkaline solution gave *p*-bromoaniline in a yield amounting to 52 per cent. of the theoretical, but no other pure substance was isolated. The formation of small quantities of a blue dye similar to that obtained by the reduction of nitroglyoxaline was observed.

4-p-*Bromobenzeneazo-2-methylglyoxaline-5-carboxylic Acid.*

This substance was prepared in a similar manner to the 2-phenyl homologue. Starting with 7·52 grams of 2-methylglyoxaline-4:5-dicarboxylic acid, the precipitate which formed was collected (*A*) and the filtrate acidified with hydrochloric acid, when 2 grams of pale orange crystals were obtained. These dissolved somewhat sparingly in alcohol, and separated in glistening, orange needles. The precipitate (*A*) was suspended in water and acidified with hydrochloric acid, when it gave 7 grams of an orange powder, consisting of a mixture of the azo-compound and the unchanged acid. Separation was effected by extraction with, and crystallisation from, alcohol, in which the original acid is practically insoluble, when 5·4 grams of 2-methylglyoxalinedicarboxylic acid were recovered unchanged. In a later experiment, the reaction was allowed to proceed for several hours, but although the yield of the product was larger, it was much darker in colour and more difficult to purify. The ultimate filtrates from the recrystallisation from alcohol yielded a small proportion of a product approximating in composition to 4:5-bis-*p*-bromobenzeneazo-2-methylglyoxaline, but owing to the ease with which resinification took place, it was not obtained pure.

4-p-*Bromobenzeneazo-2-methylglyoxaline-5-carboxylic acid* separates from alcohol, in which it is somewhat sparingly soluble, in orange needles containing $\frac{1}{2}H_2O$. It is very sparingly soluble in water, and dissolves in concentrated sulphuric acid with the production of an orange-red coloration. On heating, it darkens rapidly above 160° (Found: loss at 60° in a vacuum = 3·2. $\frac{1}{2}H_2O$ requires 2·8 per cent. In dried material, C = 43·0; H = 3·2; N = 17·8; Br = 25·4. $C_{11}H_9O_2N_4Br$ requires C = 42·7; H = 2·9; N = 18·1; Br = 25·85 per cent.).

Reduction.—On reduction, as described in the previous case, the evolution of carbon dioxide was again noticed. The insoluble stannichlorides, which accounted for almost the whole of the starting material, yielded 2-methyl-4-(2′-amino-5′-bromophenyl)-5-glyoxalone hydrochloride, which melted at 272° (corr.), the mixture with the reduction product of 4-*p*-bromobenzeneazo-2-methylglyoxaline melting at 272° in the same bath (Found: C = 39·2; H = 3·9; N = 13·7. $C_{10}H_{10}ON_3Br,HCl$ requires C = 39·4; H = 3·85; N = 13·8 per cent.).

The identity was further confirmed by isolation of the base and picrate, and by comparison of the reactions of the bases from the two sources, both of which gave the reactions previously described (T., 1920, **117**, 677).

2-p-*Bromobenzeneazoglyoxaline-4:5-dicarboxylic Acid.*

This was prepared in the manner already described. The precipitate, which formed fairly rapidly, was collected after three hours. The filtrate, on acidification, gave a further quantity of the azo-compound admixed with the unchanged acid. The precipitate was boiled with water containing a little sodium carbonate, leaving a dark brown residue insoluble in sodium carbonate or sodium hydroxide.* The extract, on acidification, gave an orange-red precipitate, which, after boiling with alcohol and drying, darkened above 200° and melted and effervesced at 250° (corr.). It dissolved but sparingly in alcohol, and separated in bunches of minute, red needles, which melted at the same temperature and contained $1C_2H_6O$ (Found, in air-dried material: C = 40·9; H = 3·7; N = 14·6; Br = 21·3; loss at 100° in a vacuum = 11·5. $C_{11}H_7O_4N_4Br,C_2H_6O$ requires C = 40·5; H = 3·4; N = 14·55; Br = 20·75; C_2H_6O = 12·0 per cent. In dried material: C = 39·3; H = 2·4. $C_{11}H_7O_4N_4Br$ requires C = 38·95; H = 2·1 per cent.).

Reduction.—The reduction was carried out as in the previous instances. The decolorised solution from 4 grams of the azo-deriv-

* This is possibly 2:4:5-tris-*p*-bromobenzeneazoglyoxaline.

ative, on dilution with water, gave a precipitate amounting to 3 grams. This dissolved sparingly in water, dilute acids, and the usual organic solvents, but rather more readily in 50 per cent. acetic acid, from which it separated in clusters of minute needles. On heating, these darkened rapidly above 190° and effervesced at 203° (corr.) (Found: loss at 100° in a vacuum = 2·9. $C_{11}H_9O_4N_4Br,\frac{1}{2}H_2O$ requires $H_2O=2·6$ per cent. In dried material: C=39·1, 39·0; H=3·1, 3·0; N=16·2, 16·3; Br=23·8. $C_{11}H_9O_4N_4Br$ requires C=38·7; H=2·7; N=16·4; Br=23·4 per cent.).

In aqueous solution, the following characteristic reactions were observed: with warm dilute hydrogen peroxide, development of a reddish-brown coloration; with warm ferric chloride, a turbid, orange solution; with warm dilute nitric acid, a bright yellow coloration, whilst silver nitrate and Fehling's solution were reduced on warming.

The composition and properties therefore indicate that the substance is 2-p-*bromobenzenehydrazoglyoxaline*-4:5-*dicarboxylic acid.*

The solution remaining after precipitation of the above substance was freed from tin and evaporated to dryness, leaving 0·7 gram of residue. From this, by suitable means, 0·35 gram of *p*-bromoaniline was isolated and identified, whilst the residual solution then developed a strong odour of ammonia on warming with alkali.

Nitration of 2-Phenylglyoxaline-4:5-dicarboxylic Acid.

A solution of 2 grams of the acid in a mixture of 4 c.c. of nitric acid (D 1·4) and 4 c.c.of sulphuric acid was heated for eight hours on the water-bath, then cooled, poured on ice, and the precipitated product crystallised from 120 parts of boiling water. It separates in small needles, very sparingly soluble in cold water or the usual organic solvents, but readily so in alkalis, with the production of a red coloration. On heating, the substance effervesces at 266° (corr.) (Found: C=47·9; H=2·6; N=15·3. $C_{11}H_7O_6N_3$ requires C=47·7; H=2·5; N=15·2 per cent.).

The composition of the product therefore indicates that nitration has taken place only in the benzene nucleus, and that, as in the case of glyoxalinedicarboxylic acid and its 2-methyl homologue, there is no tendency for displacement of the carboxylic by the nitro-group. In view of the predominating negative character of the glyoxalinedicarboxylic acid substituent, the substance is in all probability 2-m-*nitrophenylglyoxaline*-4:5-*dicarboxylic acid.*

The corresponding *amino-acid* was obtained by reduction with

sodium hyposulphite in alkaline solution. It dissolves readily in dilute mineral acids, but very sparingly in the usual organic solvents, 50 per cent. acetic acid, or hot water, from which it separates in powdery crystals containing $2H_2O$. After treatment with nitrous acid, it develops a deep red coloration on addition to sodium β-naphthoxide (Found: loss at 110° = 12·4. $C_{11}H_9O_4N_3,2H_2O$ requires $H_2O = 12·7$ per cent. In dried material: N = 16·2. $C_{11}H_9O_4N_3$ requires N = 16·2 per cent.).

WELLCOME CHEMICAL RESEARCH LABORATORIES.

[*Received, January 14th*, 1921.]

PRINTED IN GREAT BRITAIN BY THE CORNWALL PRESS, LTD.,
PARIS GARDEN, STAMFORD STREET, LONDON, S.E. 1.